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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,518	03/09/2001	Gary Van Nest	377882001100	9215

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,518	VAN NEST, GARY	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-16,19-25 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-13,16,19-23 and 28* is/are rejected.

7)☒ Claim(s) *14,15,24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is a reply to the Paper filed 1 March 2005 in response to the Non-Final Office Action mailed 1 October 2004. Claims 1-6, 8-16, 18-25, 27 and 28 were considered in the 1 October Office Action. Claims 18 and 27 were canceled and claims 1, 10 and 20 were amended in the 1 March Paper. Claims 1-6, 8-16, 19-25 and 28 are pending and under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 102

Claims 1, 2, 8-11, 16, 19-21 and 28 **stand rejected** under 35 U.S.C. 102(b) as being anticipated by Hutcherson *et al.* (1997) US Patent No. 5,663,153.

It was established in the previous Office action (beginning at page 2) that Hutcherson *et al.* teaches a method for preventing, reducing the severity of or reducing the recurrence of a symptom of HSV infection comprising each of the limitations of the instant claims.

In response to the *prima facie* case of record, Applicant has amended claim 1 to recite that the ISS is administered to an individual exposed to herpes simplex virus. Applicant asserts that Hutcherson *et al.* does not anticipate the amended claims because Hutcherson provides no definitive information on when treatments took place relative to infection and clearly does not teach that the administration occurs prior to 3 days after HSV exposure (page 8 of the 1 March Paper).

This argument has been fully considered but is not deemed persuasive because it is based on an overly narrow construction of the claims. The claims require that the ISS be administered

to "an individual exposed to herpes simplex virus" and that the "composition be administered prior to three days after virus exposure in an amount sufficient to prevent a symptom of herpes simplex virus infection". In the remarks, Applicant acknowledges that Hutcherson teaches treating HSV using an oligonucleotide containing 5'-CG-3' at column 10, lines 26-49 and column 12, lines 4-6 and Example 11, but argues, "this disclosure does not teach that the oligonucleotide is administered prior to 3 days after HSV exposure".

As stated in the previous Office Action, the claims encompass administration of the CpG at any point prior to three days after virus exposure, including prior to virus exposure. It is further noted that the base claim does not recite "prior to 3 days after HSV exposure" as applicant asserts (emphasis added). Instead the claim merely recites "prior to three days after virus exposure" and there is no definite article or adjective "said" preceding "virus" to indicate reference to any particular virus exposure. In view of the fact that "viruses" are continuously present in any environment and all organisms are continuously exposed to viruses, essentially any point in time is prior to three days after exposure to "a virus". Given that the individuals to which the 5'-CG-3' oligonucleotide was administered in the method of Hutcherson had clearly been "exposed to HSV" and "prior to three days after virus exposure" can reasonably be construed as any point in time, the method of Hutcherson *et al.* anticipates the method of claim 1 and, for the reasons stated in the previous Office Action, the claims depending therefrom.

Applicant has amended claims 10 and 20 to recite that administration of the composition is parenteral and urges, "Hutcherson describes only topical or local administration of the oligonucleotide to the site of infection. Hutcherson does not teach parenteral administration" (third paragraph on page 8 of the Remarks). However, the passage cited by applicant in support

of the limitation (fourth full paragraph on page 37) states, "[p]arenteral routes of administration include, but are not limited to...intradermal (ID) routes" (emphasis added). Thus, the specification teaches that ID is clearly within the scope of parenteral administration. Hutcherson teaches ID administration of the composition (see especially the first full paragraph in column 12) and therefore anticipates the limitation. Furthermore, the passage cited by Applicant clearly indicates that parenteral administration is not limited to the routes recited in the specification. As Stedman's online medical dictionary defines parenteral as "by some other means than through the gastrointestinal tract", even the topical administration exemplified in Hutcherson is within the broadest reasonable interpretation of the claimed method.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §102(b) as anticipated by Hutcherson *et al.*

Rejection of claims 1-4 and 9 under 35 U.S.C. 102(e) as being anticipated by Wagner *et al.* US PG Pub No. 2004/0030118 is **withdrawn** in view of the amendment of the claims such that the polynucleotide comprising an ISS is administered to an individual exposed to a herpes simplex virus. Wagner *et al.* does not teach that the individual treated should have been exposed to HSV.

Claim Rejections - 35 USC § 103

Rejection of claims 10-13, 16, 19-23 and 28 under 35 U.S.C. 103(a) as being unpatentable over Wagner *et al.* in view of Hutcherson *et al.* is **withdrawn**. Applicant's

arguments are persuasive. Modifying the method of Wagner *et al.* to administer the therapeutic oligonucleotide to an individual during an active infection as taught by Hutcherson *et al.* would be inconsistent with the principle of immune system remodeling prior to antigen exposure as taught by Wagner *et al.*

New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in reciting, "said composition is administered prior to three days after virus exposure". It is unclear what "virus exposure" is being referred to in the claim. As discussed above, there is no article or adjective preceding "virus" in the claim, thus it is unclear whether the limitation is referring to exposure to HSV or if the claim broadly encompass administration prior to three days after exposure to any virus. Therefore, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 9-13, 16, 19-23 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner *et al.* US PG Pub No. 2004/0030118 (previously made of record) in view of Rosenthal *et al.* (1997) *Clin. Infect. Dis.* 24:135-139.

Wagner *et al.* teaches a method of inducing immune remodeling based on the generation of immune cells through the administering CpG oligonucleotides (see especially paragraph [0075]). In paragraph [0077], Wagner *et al.* teaches that the subject receiving CpG treatment may be exposed passively to an antigen to which the subject is exposed from the environment. As discussed above, the broadest reasonable interpretation of claim 1 includes administration of the CpG at any point prior to three days after virus exposure, including prior to virus exposure in accordance with the teachings of Wagner *et al.* Wagner *et al.* also teaches that the source of the antigen can be HSV 1 and 2 (see especially paragraph [0083]), that the oligonucleotide comprises a phosphate backbone modification (see especially paragraph [0045]) and is between 6 and 200 nucleotides in length (see especially paragraph [0044]), that a herpes simplex virus antigen is not coadministered in conjunction with the composition (see especially paragraph

[0120]), and that the individual is a human (see especially paragraph [0030]). Wagner *et al.* thus teaches a method comprising all of the limitations of independent claims 1, 10 and 20 except that the composition is administered to an individual exposed to or infected with herpes simplex virus.

However, the specification defines "infected individual" as "an individual who has been infected by a herpes virus. For *alphaherpesvirinae,* symptoms of infection include seropositivity". Rosenthal *et al.* teaches that at least 62% of adolescents 12 to 22 years of age have been exposed to HSV as evidenced by seropositivity for HSV-1 or HSV-2 (see throughout, especially the Abstract). This teaching evidences the very high incidence of exposure to HSV in the general population. One would be motivated to treat individuals exposed to and infected with HSV, as these terms encompass any seropositive individual, given the very high incidence of seropositivity and the understanding that it is generally desirable to treat as large a segment of the population as possible.

Although it is acknowledged above that modifying the method of Wagner *et al.* to administer the therapeutic oligonucleotide to an individual during an active infection, as taught by Hutcherson *et al.*, would be inconsistent with the principle of immune system remodeling prior to antigen exposure as taught by Wagner *et al.*, the instant rejection is not inconsistent with the principles of Wagner *et al.* The principle of Wagner *et al.*, as stated by Applicant is to stimulate an antigen-specific immune response by administration of CpG oligonucleotides prior to antigen exposure. Seropositivity is an indicator of infection at some point in an individual's lifetime and does not require that antigen is continuously present in the individual. Therefore, treating a seropositive individual according to the method of Wagner *et al.* in order to provide an

enhanced immune response to HSV challenge, wherein the individual is subsequently exposed to viral antigen, is consistent with the method of Wagner *et al.* and one would be motivated to do so in view of the very high incidence of seropositivity in the general population. Thus, the methods of claims 1, 10, 16 and 20, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings in view of the demonstrated immunostimulatory effects of the oligonucleotides of Wagner *et al.*

Wagner *et al.* further teaches the method wherein the ISS comprises the sequence 5'-GACGTTCC-3' according to claims 2-4, 11-13 and 21-23 (see paragraph [0149], especially SEQ ID NO: 71) and wherein the virus is HSV-2 (*Id.*) according to claims 9, 19 and 28.

For these reasons, the invention of claims 1-4, 9-13, 16, 19-23 and 28, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 14, 15, 24 and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER